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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/630,215	08/01/2000	John F. O'Connor	54205-A-PCT-US/JPW/SHS/MV	7218

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EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/630,215	Applicant(s) O'CONNOR ET AL.	
	Examiner Gailene R. Gabel	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/17/03 has been entered.

Amendment Entry

2. Applicant's amendment and response filed 3/17/03 in Paper No. 15 is acknowledged and has been entered. Claim 68 has been cancelled. Accordingly, claims 58-67 are pending and are under examination.

Rejections Withdrawn

3. Rejections of claim 68 under 35 U.S.C. 112 are now moot in light of Applicant's cancellation of the claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 58-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 58 is indefinite in reciting, "EPMI-hCG". Acronyms or abbreviations must be fully defined and recited at least one time in a set of claims.

Claim 58 is vague and indefinite in reciting, "a first antibody which binds to the EPAMI-hCG that is recognized by the B152 antibody" because it is unclear as to whether the first antibody or the EPAMI-hCG is recognized by the B152 antibody.

The same analogous comments and problems in claim 58 apply to claims 62, 63, and 67.

Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 58-67 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods relying on monoclonal antibody B152 as the antibody which specifically binds to EPAMI-hCG, does not reasonably provide enablement for any other antibody which binds to EPAMI-hCG. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons of record.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 58-67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of using an antibody that binds to EPAMI-hCG for use in a method of predicting pregnancy outcome in a subject. Such antibody has not been properly described in the specification so that one skilled in the art can make and use the invention as claimed.

In order to make the antibody as claimed, first, a compound fitting the description must be identified and/or isolated. In this case, the specification fails to provide a written description of the claimed antibody nor does it provide evidence that Applicant has ever identified such antibody. Additionally, the chemical structure of EPAMI-hCG from which the antibody is produced, has not been characterized by the specification nor has its full length sequence been fully identified, defined, and disclosed. Without specific description of EPAMI-hCG or an epitope upon which the claimed antibody binds for use in a method of predicting pregnancy outcome, one skilled in the art would not be able to make and use the antibody in the method as claimed. Unlike linear amino acid

epitopes, which can be readily synthesized in vitro and against which other antibodies can be readily made, carbohydrate epitopes are more complex and difficult to synthesize. According to Knight, "the structure of carbohydrates is much more complex than that of proteins. Dwek further likens the task of sequencing a carbohydrate to "simultaneously sequencing 40-50 proteins". Because carbohydrate structures are a branching series of linked rings, they can combine in many more ways than can linear peptide chains. One skilled in the art would reasonably conclude that, even if one has known that B152 epitope comprised carbohydrate moieties, the synthesis of potential carbohydrate moieties would require undue experimentation. The mere recitation of an antibody capable of binding EPAMI-hCG does not adequately define an antibody for use in the claimed method.

Knight also teaches the unpredictability of knowing the exact structure found therein as well as "microheterogeneity" in the form of discrete subsets- glycoforms- of a glycoprotein which have different physical and biochemical properties. According to Rademacher, Parekh, and Dwek, "any given glycoprotein that consists of different glycoforms will ... have a composite activity, reflecting a weighted average of the activity and incidence of each glycoform". One skilled in the art would then reasonably conclude that these different physical and biochemical properties encompass different epitopes upon which an antibody can bind. Not only have the glycoforms on hCG not been fully characterized, but neither the glycoisoforms, thereof.

The prior art of record clearly shows evidence of unpredictability as to the presence or nature of EPAMI-hCG that is found in early pregnancy. Therefore, because

the prior art has been shown to be unpredictable as to its nature, and because the specification lacks proper guidance or direction as to how to make the antibody thereto, as claimed, when the compound used to make such antibody has not been positively identified, one skilled in the art can not make and use the invention as claimed without undue experimentation.

The instant claims fail to meet written description to show possession of the claimed invention because the composition comprising the antibody for use in the method, as claimed, has not been adequately described. Even though the level of skill and knowledge in the art of antibodies at the time of filing is such that production of antibodies against a well-characterized antigen was conventional, and antibody technology is a mature technology where the level of skill is high and advanced, due to the lack of a description of EPAMI-hCG to which the antibody binds, the antibody cannot be characterized by its binding function. The specification only exemplifies B152 antibody which specifically binds to an EPAMI-hCG, and asserts that another antibody that binds the same epitope in EPAMI-hCG can be used in the method of predicting pregnancy outcome as claimed. Antibodies contain an effector portion which is the constant region, and a variable region that contains the antigen binding sites in the form of complementarity determining regions and the framework regions. The sequences of constant regions as well as the framework regions from a variety of species are known and published in the art; however, the variable region that contains the antigen binding sites varies depending on the specific antigen, and since the antigen in this instant, is not fully disclosed or properly described in the specification, a complete antibody

binding to EPAMI-hCG fails to meet written description to show possession of the antibody.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 58-67 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 53, 59, 60, 65, 71, 72, and 77-82 of copending Application No. 09/017, 976, now US Patent 6,500,627, for reasons of record.

Response to Arguments

8. Applicant's arguments filed 3/17/03 have been fully considered but they are not persuasive.

A) Applicant contends that no structural knowledge of an epitope is required to practice the claimed invention. According to Applicant, the antibody used can be made

in view of the specification, according to routine procedures of immunization, hybridoma production, and screening. Applicant points to Exhibit 9 for support that no structural knowledge of an epitope is required in antigen-antibody interactions and to Exhibit 8 wherein assay binding outcomes using two antibodies are exemplified for further support, that no structural knowledge of epitopes is required to determine whether or not two antibodies bind the same region on hCG.

In response to Applicant's contention that no structural knowledge of an epitope is required to make an antibody such as that used in the claimed method, and that ordinary skill in the art would readily acknowledge that the claimed antibody can be produced using only routine methods well known in the art, it is well established that even though level of skill and knowledge in the art at the time of filing was such that production of antibodies even those against a well characterized antigen, i.e. αhCG, βhCG, FSH, is well known and conventional, Applicant has not demonstrated nor has he provided sufficient guidance, that a particular conclusory antibody that identifies that conserved epitope of EPAMI-hCG that is universal to both the claimed antibody and B152 is known, well-characterized, or sequenced so as to enable the claimed invention. To reiterate, the specification provides general teaching of how such antibody can be generated, selected, and used. Exhibits 8, 9, 10, and 11 also provide description and clarification of how antibodies can be selected and screened based on their binding to epitopes of a specific well-characterized antigen, i.e. αhCG, βhCG, FSH, but do nothing to further enable the antibody that recognizes and binds the same epitope of EPAMI-hCG as B152; thus, having specific binding for a universal epitope as that of B152. As

such, Applicant's arguments that such antibody can be generated and is in existence so as to render Applicant's possession of the antibody for use in the claimed method, are prophetic and speculative but not convincing. In addition, the issue at hand is not whether two antibodies can bind a same region in an antigen for use in an assay but whether another antibody specific for binding with an epitope of EPAMI-hCG, but distinct from B152 which is specific for the same epitope, has been generated for use in the method as claimed.

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday from 7:00 AM to 4:30 PM. The examiner can also be reached on alternate Fridays from 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 308-9933. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel

Patent Examiner
Art Unit 1641

8/8/21/03

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641